IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Peter J. Sims

Serial No.: 09/020,393 Art Unit: 1644

Filed: February 9, 1998 Examiner: P. Gambel

For: *COMPOSITIONS AND METHODS TO INHIBIT FORMATION OF THE C5B-9 COMPLEX OF COMPLEMENT*

Assistant Commissioner for Patents
Washington, D.C. 20231

APPEAL BRIEF

Sir:

This is an appeal from the final rejection of claims 10-12, 16 and 17 and withdrawal of claims 1-9, 13-15, and 18-35 in the Office Action mailed January 28, 2000 in the above-identified patent application. A Notice of Appeal was filed on June 28, 2000. A check in the amount of $155 for the filing of this Appellants' Brief is also enclosed along with a petition for an extension of time for four months, up to and including December 28, 2000, and the appropriate fee for a small entity.

(1) REAL PARTY IN INTEREST

The real parties in interest of this application are the Oklahoma Medical Research Foundation and Blood Center Research Foundation, Inc., the assignees.

(2) RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences known to appellant, the undersigned, or appellant's assignee which directly affects, which would be directly affected by, or which would have a bearing on the Board's decision in this appeal.

(3) STATUS OF CLAIMS ON APPEAL

Claims 1-35 are pending. Claims 1-35 were restricted into thirty two groups in an Office Action mailed February 4, 1999. This requirement was traversed and a petition for reconsideration mailed on November 8, 1999. A Decision was mailed March 17, 2000, and received December 28, 2000. Claims 10-12, 16 and 17 were finally rejected in the Office Action mailed January 28, 2000.

(4) STATUS OF AMENDMENTS

The text of each claim on appeal, as amended in the Amendment mailed May 30, 2000, is set forth in the Appendix to this Appeal Brief. As indicated in the Advisory Action mailed June 14, 2000, and received December 28, 2000, the amendment was to be entered upon filing of an appeal.

(5) SUMMARY OF THE INVENTION

Compounds modulating CD59 mediated complement activity which are based on the identification of the hu CD59 amino acid residues which serve as the binding site for CD59-C9 interactions are described and claimed. These residues correspond to amino acid residues 42-58, and bind to the region of C9 corresponding to human 334-418, more specifically, between amino acid residues 359 and 384. The claim compounds are derived using this basic amino acid sequence and corresponding three dimensional structure within the protein using any of several techniques known to those skilled in the

art, including rational drug design using computer data bases and modeling of peptide/protein-ligand binding, antibodies and anti-idiotypic antibodies generated to the proteins or peptides containing this peptide sequence, and modified peptides. Those compounds imitating the structure and/or function of the peptide region are referred to as "peptidomimetics", and include small molecules which present the surface exposed side chains in these amino acids in the same relative positions, compounds identified by combinatorial chemistry techniques which bind to the active portions of human C9, as well as modified peptides. (page 6, line 16 to page 7, line 3)

The compounds can be used to inhibit complement by binding to C9 analogously to CD59, or to maintain complement inhibition, by blocking CD59 binding to C9. The compounds can be administered locally or systemically in any suitable carrier in an amount effective to either inhibit complement or block the inhibition of complement, in a patient in need of treatment thereof. (page 7, lines 3-9)

The claims are drawn to a molecule mimicking the region of human CD59 which is both species specific (i.e., unique to human) (page 12, lines 7-13) and which binds to C9, thereby inhibiting complement activation mediated by formation of the human C5b-9 complex (page 13, lines 21-24). There is an important limitation in the claims: the compound must structurally mimick human CD59 amino acid resides 42-58 when these amino acids have the same spatial orientation as when present in the intact molecule (page 19, lines 8-16). The compound must bind specifically to amino acids 359 to 384 of human C9 (page 43, line 23 to page 45, line 13).

(6) ISSUES ON APPEAL

The issues presented on appeal are:

(1) whether claims 10-12 and 16-17 are properly rejected under 35 U.S.C. §112, second paragraph, on the basis that the claimed invention is not clearly defined in the application;

(2) whether claims 10-12 and 16-17 are properly rejected under 35 U.S.C. §112, first paragraph, on the basis that the claimed invention is not clearly enabled by the application;

(3) whether claims 10-12 and 16-17 are disclosed by under 35 U.S.C. §102(b) or obvious under 35 U.S.C. §103 over U.S. Patent No. 5,550,108 to Sims, et al.;

(4) whether claims 10-12 and 16-17 are obvious under 35 U.S.C. §103 over the combination of U.S. patent No. 5,550,108 to Sims and Chang, et al., J. Biol. Chem.269(42), 26424-26430 (1994); and

(5) whether the examiner should have considered the other claims drawn to the same subject matter, as grouped together in the restriction requirement mailed February 4, 1999, claims 10-12, 16, 17, 27-29, and 33-35.

(7) GROUPING OF CLAIMS

The claims do not stand or fall together. The claims must be considered separately because they are drawn to different chemical entities - indeed this was the basis for requiring that appellant elect a single species from the species defined by claims 10-12, 16, 17, 27-29, and 33-35, which fall within the generic claim 10.

Claim 10 is drawn to a method for inhibiting human C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition comprising a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules having the structure and function of human

CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9.

Claim 11 defines the species of peptidomimetic as a small molecule which binds specifically to amino acids 359 to 384 of human C9.

Claim 12 defines the species of peptidomimetics as an antibody.

Claim 13 defines the peptidomimetic as a chimeric peptide which includes the amino acids 42 to 58 of the human sequence of CD59. Claim 14 defines the peptidomimetics as a covalently cyclized peptide comprising human CD59 amino acid residues 42 to 58. Claim 15 defines the peptidomimetic as a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of human CD59. Claim 18 defines the peptidomimetic as comprising the side chains of human CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the spatial orientation and alignment of hu CD59. Claim 19 defines the peptidomimetic of claim 18 wherein the spatial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are deduced by NMR structure determination.

Claims 16 and 17 are drawn to a method of treatment (claim 17) and inclusion in the composition of a pharmaceutically acceptable carrier for administration to patients in need thereof.

Accordingly, at a minimum, the claims must be examined separately based on whether or not they require further limitations as to the chemical structure of the peptidomimetic, or go to the method of use. As to the peptidomimetics, these should be examined separately for both enablement and with regard to the prior art, which does not show inhibitors as defined by the claims.

(8) ARGUMENTS

(i) The Invention

The complement system is a complex interaction of plasma proteins and membrane cofactors which act in a multi-step, multi-protein cascade sequence in conjunction with other immunological systems of the body to provide immunity from intrusion of foreign cells. The classic complement pathway involves an initial antibody recognition of, and binding to, an antigenic site (SA) on a target cell. This surface bound antibody subsequently reacts with the first component of complement, C1q, forming a C1-antibody complex with Ca^{+2}, C1r, and C1s which is proteolytically active. The C5b,6,7 complex binds C8 at the surface of the cell, which may develop functional membrane lesions and undergo slow lysis. Upon binding of C9 to the C8 molecules in the C5b,6,7,8 complex, lysis of bacteria and other foreign cells is rapidly accelerated.

The C5b-9 proteins of the human plasma complement system have been implicated in non-lytic stimulatory responses from certain human vascular and blood cells. The capacity of C5b-9 to modify membrane permeability and to selectively alter ion conductance is thought to elicit these non-lytic responses from human cells. These effects of complement proteins C5b-9 on platelet and endothelial cells alter the normal regulation of the enzymes of the plasma coagulation system at these cell surfaces. This interaction between components of the complement and coagulation systems at the surface of blood platelets and endothelium can generate inflammatory and chemotactic peptides at sites of vascular thrombus formation and may contribute to the altered hemostasis associated with immune disease states.

Human (hu) CD59 antigen is a 18-21 kDa plasma membrane protein that functions as an inhibitor of the C5b-9 membrane attack complex (MAC) of human complement. CD59 interacts with both the C8 and C9 components of MAC during its assembly at the cell surface, thereby inhibiting formation of the membrane-inserted C9 homopolymer responsible for MAC cytolytic activity. CD59's inhibitory activity is dependent upon the species of origin of C8 and C9, with greatest inhibitory activity observed when C9 is from human or other primates. Analysis of the physical association of CD59 with components of MAC suggested that separate binding sites for CD59 are contained within the α-chain of hu C8 and within hu C9. The complement-inhibitory activity of CD59 is species-selective, and is most effective towards C9 derived from human or other primate plasma. The species-selective activity of CD59 was used to map the segment of human C9 that is recognized by this MAC inhibitor, using recombinant rabbit/human C9 chimeras that retain lytic function within the MAC. These experiments indicated that the CD59 recognition domain was contained between residues 334-415 in human C9, as described in PCT/US96/17940 "C9 Complement Inhibitor" by Oklahoma Medical Research Foundation.

Compounds modulating CD59 mediated complement activity, compositions including these compounds, and methods of making and using the compounds are disclosed, which are based on the identification of the hu CD59 amino acid residues which serve as the binding site for CD59-C9 interactions. These residues correspond to amino acid residues 42-58, and bind to the region of C9 corresponding to human 334-418, more specifically, between amino acid residues 359 and 384. Compounds can be derived using this basic amino acid sequence and corresponding three dimensional

structure within the protein using any of several techniques known to those skilled in the art, including rational drug design using computer data bases and modeling of peptide/protein-ligand binding, antibodies and anti-idiotypic antibodies generated to the proteins or peptides containing this peptide sequence, and modified peptides. Those compounds imitating the structure and/or function of the peptide region are referred to herein as "peptidomimetics", and include small molecules which present the surface exposed side chains in these amino acids in the same relative positions, compounds identified by combinatorial chemistry techniques which bind to the active portions of human C9, as well as modified peptides.

The compounds can be used to inhibit complement by binding to C9 analogously to CD59, or to maintain complement inhibition, by blocking CD59 binding to C9. The compounds can be administered locally or systemically in any suitable carrier in an amount effective to either inhibit complement or block the inhibition of complement, in a patient in need of treatment thereof.

The application provides an extensive disclosure of the methods and materials required to make these peptidomimetics. The critical features of the CD59 and C9 which must interact to provide species specific inhibition are described in the application at pages 12-13. Chimeric proteins are described at page 13, line 26 to page 14, line 6. Antibodies to amino acids 42-58 of CD59 and antibodies to amino acids 359-384 of hu 9 are described at page 14, line 7 to page 17, line 19, and demonstrated in the examples, as discussed below. Identification of compounds by combinatorial chemical is described at pae 17, line 20 to page 18, line 26. Rational drug design and suitable computer software for use therein is described at page 18, line 27 to page 24, line 13. Methods for synthesis

of these compounds are described at page 24, line 14 to page 27, line 9. Methods of treatment are described at page 28, line 3 to page 29, line 11. The examples further demonstrate the production and testing of both specific antibodies and modified peptides that are useful in blocking binding of C9 to CD59. Specifically, example 1, at page 28, line 15 to page 39, line 30, describes making CD59 chimeric proteins which inhibit C9 binding. Example 2, at page 40, line 1 to page 43, line 22, describes making site directed mutations in C9 peptides and chimeric proteins to create inhibitors which block binding to C9/CD59. Example 2, page 43, lines 23-29, describes making antibodies to C9 peptide 359-384. The results at pages 44-48 and accompanying figures demonstrate that these peptides, chimeric proteins and antibodies were effective as specific specific complement inhibitors.

(ii) Rejections Under 35 U.S.C. § 112, first pararaph

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*See, e.g.*, Genentech, Inc. v. Novo Nordisk A/S, 108 F3d at 165, 42 USPQ2d at 1004 (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also In re Fisher, 427 F.2d at 839, 166 USPQ at 24; United States v. Telectronics, Inc., 857 F.2d 778 (Fed. Cir. 1988); In re Stephens, 529 F.2d 1343 (CCPA 1976)). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (M.I.T. v. A.B. Fortia, 774 F.2d 1104 (Fed. Cir. 1985)). In addition, as

affirmed by the Court in Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524 (Fed. Cir. 1987), a patent need not teach, and preferably omits, what is well known in the art.

Whether making or using the invention would have required undue experimentation, and thus whether the disclosure is enabling, is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. In cases that involve unpredictable factors, "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' Atlas Powder Co. v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

> The test is not merely quantitative, since a considerable amount of experiment is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.
>
> Ex parte Jackson, 217 USPQ 804, 807 (1982)

As stated in the MANUAL OF PATENT EXAMINING PROCEDURE §2164.04 (7th ed. 1998), *citing* In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993), the examiner has the initial burden to establish a reasonable basis to question the enablement of the application.

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must be taken as being in compliance with the enablement requirement** of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.
>
> *Id.* at § 2164.05 (emphasis added).

In this case, the examiner has consistently relied on conclusory statements without putting forth specific reasons describing why the claims are not enabled by the specification. The patent examiner cannot just assert that the application is not enabled. As stated in In re Marzocchi at 439 F.2d 220 (CCPA 1971:

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made [, enablement under § 112, first paragraph], to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise,

there would be no need for the Appellant to go to the trouble and expense of supporting his presumptively accurate disclosure.

Id. at 224.

The MPEP instructs examiners to make specific findings of *facts* to rebut Appellants' presumption and "specifically identify what information is missing and why one of skill in the art could not supply the information without undue experimentation." MPEP at § 2164.05. The examiner should provide references to support a *prima facie* case of lack of enablement. *Id.*

There is no legal requirement that an inventor have actually reduced the invention to practice prior to filing. M.P.E.P. at § 2164.02, *citing Gould v. Quigg*, 822 F.2d 1074, 3 U.S.P.Q.2d 1302 (Fed. Cir. 1987). "The specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation." *Id.* In this case, however, the specification contains examples of at least three different examples of the claimed compositions: peptides, chimeric proteins, and antibodies.

It is well established law that the claims should be interpreted in view of the specification - in this case, the extensive disclosure in the specification at pages 11 and 13-27, which describes molecules including proteins, antibodies, compounds identified using combinatorial, and compounds identified by rational drug design, using the guidelines provided based on the discovery that one short peptide sequence of human CD59 alone is responsible for the species-specific binding of CD59 to inhibit formation of the C5-b9 complex, using the standard of one skilled in the art.

With computer programs that can be downloaded readily from the internet, and the entire amino acid sequences of the relevant molecules (CD59 and C9) being known, it would be routine to create a three dimensional structure as claimed. The invention resides in knowing which portion of these two structures are critical for **species-specific binding.** .

(iii) Rejections Under 35 U.S.C. § 112, second pararaph

As the Board is aware the standard for enablement and clarity is what one of skill in the art, would understand from the claims in view of the specification. Those skilled in the art would learn from the extensive examples that a very small region of human CD59 is responsible for CD59 species-specific role as a complement inhibitor. Indeed, the data at page 47 shows just how specific this role is, since substitution of amino acids to create the structure present in the analogous region of rabbit CD59 destroys the ability of the molecule to inhibit C5b-9 complex formation. The computer programs available at the time of filing provide extensive guidance once the data regarding the exact composition and spatial orientation and alignment provided by applicants has been entered into the program. Moreover, the assays can be used as a final determining factor – since the requirements for inhibition are so stringent, failure to inhibit formation of the human C5b-9 complex can be used as a rapid, simple screen. The requirement of a specific functional activity has been incorporated into the independent claim.

Accordingly, the claims are definite to those skilled in the art based on the specification.

(iv) Rejections Under 35 U.S.C. § 102

Claim 10 is drawn to a method for inhibiting human C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition comprising a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules having the structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9.

Sims does not identify CD amino acid residues 42-59 nor that this region binds to amino acid residues 359-384, either explicitly nor implicitly. This fact simply was not known until the studies described in this application were performed. It is not enough to stay that because antibodies which bind to CD59, or C9, are disclosed, that these antibodies are specific for these regions.

Sims et al. is based on the discovery that CD59 inhibits complement activation, not just hemolysis, and notes that antibodies to C9 can be used to inhibit CD59 activity. There is no disclosure of what region of CD59 imparts species-specificity. Merely because there may be an antibody which binds to C9 does not mean that it mimicks the region of CD59 which is in issue; in fact, absent making the antibody by immunization with this region, and then screening for efficacy in preventing human CD59 activity, it is extremely unlikely that such an antibody could be obtained. See in particular page 47 in this regard. Both CD59 and C9 are large proteins with complex tertiary structures. One cannot obtain specific antibodies just by immunization with the entire protein. One especially cannot obtain antibodies that block the *species-specific* binding, absent knowing which region of the protein is responsible for this activity. One had to

immunize with the specific region of the protein, in order to obtain antibody that blocked the hemolytic activity of the human C5b-9 complex but not the rabbit C5b-9 complex.

Accordingly, Sims does not disclose nor make obvious the claimed subject matter.

(v) Rejections Under 35 U.S.C. § 103

As discussed above, Sims fails to disclose the critical region of human CD59 which must be imitated, and the region of human C9 which is bound by this species specific portion of CD59, which is essential for design and use of inhibitors of the species specific reaction between human CD59 and human C9. The structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9, is simply not taught by Siims, therefore one skilled in the art would not be led to make inhibitors based on their sequence and structure.

Chang is of no assistance in this regard. Chang identifies the region of human C9 which is bound by human CD59; not the portion of CD59 which binds. One cannot extrapolate from the information relating to human C9 to obtain information about human CD59. The identification of the critical amino acid sequence required careful analysis and many experiments, as discussed above. Absent this information, one cannot make antibodies to this region of CD59; one cannot design peptide mimics of this region of CD59; one cannot design protein chimeras of this region of CD59.

The requirement for binding to a specific region of C9 is a specific limitation of the claimed compounds. There is no teaching in the art which discloses nor leads one to this limitation, nor is it obvious. Only through careful, repetitive, and exacting studies

was it possible to determine which amino acid residues were critical to block **species specific binding.**

The U.S. Patent and Trademark Office has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177 (C.C.P.A. 1967), *In re Fine,* 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988). In rejecting a claim under 35 U.S.C. § 103, the Examiner must establish a *prima facie* case that: (i) the prior art suggests the claimed invention; and (ii) the prior art indicates that the invention would have a reasonable likelihood of success. *In re Dow Chemical Company,* 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988).

Neither criteria has been met. The prior art does not suggest which portion of human C9 is bound by human CD59, nor what structure is possessed by the claimed inhibitors or how to make them. Therefore there can be no reasonable liklihood of success. It would indeed require undue experimentation to determine which portion of human C9 is bound by CD59 and how to design inhibitors specific thereto.

The prior art must provide one of ordinary skill in the art with the motivation to make the proposed modifications needed to arrive at the claimed invention. *In re Geiger*, 815 F.2d 686, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987); *In re Lalu and Foulletier*, 747 F.2d 703, 705, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984). Claims for an invention are not *prima facie* obvious if the primary references do not suggest all elements of the claimed invention and the prior art does not suggest the modifications that would bring the primary references into conformity with the application claims. *In re Fritch*, 23 U.S.P.Q.2d, 1780 (Fed. Cir. 1992). *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989). This

is not possible when the claimed invention requires knowledge which is simply not taught by the prior art.

(vi) All of claims 10-12, 16, 17, 27-29, and 33-35 should be examined and allowed.

The examiner indicated in the restriction requirement mailed February 4, 1999, that claims 10-12, 16, and 17 were one invention drawn to the use of an antibody. He also indicated that claims 10-12, 16, 17, 27-29, and 33-35 were drawn to a different invention based on the use of an anti-idiotypic antibody. He further indicated that claims 10-11, 13, 16 and 17 were also drawn to yet another invention based on the use of a chimeric protein. He also restricted claims 10, 11, and 15-17 into yet another invention drawn to a linear peptide to inhibit formation of the human C5b-9 complex. Claims 10, 11, and 14-17 were restricted into yet another invention as drawn to the use of a cyclic peptide to inhibit formation of human C5b-9 complex. Claims 10, 11, and 16-19 drawn to a peptidomimetic compound having a specific amino acid composition were restricted into yet another invention. Claims 10, 11, 16 and 17 were restricted into yet another invention if drawn to a DNA molecule and into yet another invention if drawn to the use of a RNA molecule. Claims 10, 11, 16 and 17 were restricted into still another invention as drawn to "small molecules" which bind to human C9.

This restriction requirement was traversed, unsuccessfully, and a petition for reconsideration filed, which was denied. However, the examiner also indicated at the bottom of page 8 that he would consider rejoinder of the claims upon the allowance of a compound claim within the elected compound invention. It is clearly believed that this

restriction requirement was improper, that it should have been made as an election of species rather than a restriction requirement, and that all of claims 10-17, 27-29, and 33-35 should be considered as a single invention and allowed, the examiner having failed to establish that the claims to an antibody (which was clearly demonstrated in the specification to be made without undue experimentation, and with the claimed specificity) are not enabled, nor that they are disclosed by or obvious over the prior art.

(9) SUMMARY

Claims 10-17, at a minimum, and more properly claims 10-17, 27-29 and 33-35, should be allowed as enabled, definite, and novel and non-obvious over the prior art.

(10) CONCLUSION

None of the art discloses nor makes obvious the claimed compound which inhibits formation of the human C5b-9 complex, by imitating the structure and function of amino acid residues 42-58. The claims are both definite and enabled. Therefore the claims should be allowed.

Respectfully submitted,

Patrea L. Pabst
Reg. No. 31,284

Date: December 28, 2000
ARNALL GOLDEN & GREGORY, LLP
2800 One Atlantic Center
1201 W. Peachtree Street
Atlanta, GA 30309-3450
404-873-8794 (Phone)
404-873-8795 (Fax)

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this Appeal Brief, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date: December 28, 2000

Patrea Pabst

APPENDIX : CLAIMS ON APPEAL

1. A compound that specifically inhibits the formation of the hu C5b-9 complex selected from the group consisting of molecules structurally mimicking CD59 amino acid residues 42 to 58 when they are in a spatial orientation which inhibits formation of the hu C5b-9 complex, wherein the compound is not hu CD59.

2. The compound of claim 1, selected from the group consisting of proteins, peptides, nucleic acids, and small molecules which bind specifically to amino acids 359 to 384 of hu C9.

3. The compound of claim 2, wherein the protein is an antibody.

4. The compound of claim 2, wherein the protein is a chimeric peptide which includes the amino acids 42 to 58 of the human sequence of CD59.

5. The compound of claim 2, wherein the peptide is a covalently cyclized peptide comprising hu CD59 amino acid residues 42 to 58.

6. The compound of claim 2, wherein the composition is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of hu CD59.

7. The compound of claim 1, further comprising a pharmaceutically acceptable carrier for administration to patients in need thereof.

8. The compound of claim 1 wherein the compound is a peptidomimetic compound comprising the side chains of hu CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in an equivalent spacial orientation and alignment to that presented on the surface of hu CD59.

9. The compound of claim 8 wherein the spacial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are

equivalent to the spacial orientation and alignment deduced by NMR structure determination.

10. A method for inhibiting human C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition comprising a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules having the structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9.

11. The method of claim 10, wherein the peptidomimetic is a small molecule which binds specifically to amino acids 359 to 384 of human C9.

12. The method of claim 10, wherein the protein is an antibody.

13. The method of claim 10, wherein the protein is a chimeric peptide which includes the amino acids 42 to 58 of the human sequence of CD59.

14. The method of claim 10, wherein the peptide is a covalently cyclized peptide comprising human CD59 amino acid residues 42 to 58.

15. The method of claim 10, wherein the peptidomimetic is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of human CD59.

16. The method of claim 10, wherein the composition further comprises a pharmaceutically acceptable carrier for administration to patients in need thereof.

17. The method of claim 10, wherein the patient is in need of suppression of complement-mediated inflammation.

18. The method of claim 10 wherein the peptidomimetic comprises the side chains of human CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the spatial orientation and alignment of hu CD59.

19. The method of claim 18 wherein the spatial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are deduced by NMR structure determination.

20. A compound that specifically promotes the formation of the hu C5b-9 complex selected from the group consisting of molecules structurally mimicking C9 amino acid residues 359 to 384 when they are in a spatial orientation which promotes formation of the C5b-9 complex, wherein the compound is not hu C9.

21. The compound of claim 20, selected from the group consisting of proteins, peptides, nucleic acids, and small molecules which bind specifically to amino acids 42 to 58 of hu CD59.

22. The compound of claim 21, wherein the protein is an antibody.

23. The compound of claim 21, wherein the protein is a chimeric peptide which includes the amino acids 359 to 384 of the human sequence of C9.

24. The compound of claim 21, wherein the peptide is a covalently cyclized peptide comprising hu C9 amino acid residues 359 to 384.

25. The compound of claim 21, wherein the composition is a peptide of less than forty amino acids residues including amino acid residues 359 to 384 of hu C9.

26. The compound of claim 20, further comprising a pharmaceutically acceptable carrier for administration to patients in need thereof.

27. A method for specifically promoting hu C5b-9 complex assembly comprising administering to a patient in need thereof an effective amount of a composition to decrease CD59 inhibition of C5b-9 complex assembly wherein the composition comprises a compound selected from the group consisting of molecules structurally mimicking C9 amino acid residues 359 to 384 when they are in a spatial orientation which promotes formation of the complex, wherein the compound is not hu C9.

28. The method of claim 27, wherein the compound is selected from the group consisting of proteins, peptides, nucleic acids, and small molecules which bind specifically to amino acids 42 to 58 of hu CD59.

29. The method of claim 28, wherein the protein is an antibody.

30. The method of claim 28, wherein the protein is a chimeric peptide which include the amino acids 359 to 384 of the human sequence of C9.

31. The method of claim 28, wherein the peptide is a covalently cyclized peptide comprising hu C9 amino acid residues 359 to 384.

32. The method of claim 28, wherein the composition is a peptide of less than forty amino acids residues including amino acid residues 359 to 384 of hu C9.

33. The method of claim 27, wherein the composition further comprises a pharmaceutically acceptable carrier for administration to patients in need thereof.

34. The method of claim 27, wherein the patient is in need of complement activation.

35. The method of claim 27, wherein the composition is administered as a adjunct to tumor therapy.

TABLE OF CONTENTS